

Application No.: 09/693,204

**REMARKS/ARGUMENTS**

The Office Action mailed April 1, 2004 has been carefully reviewed and the foregoing amendments are made in response thereto. In view of the amendments and following remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. It is respectfully submitted that no new matter is presented by these amendments and respectfully request entry of the same. By these amendments, applicants do not acquiesce to the propriety of any of the examiner's rejections and do not disclaim any subject matter to which they are entitled.

***Claims Rejected Under 35 U.S.C §112, First Paragraph***

Claims 12-13 stand rejected for failing to comply with the written description requirement. In particular, in paragraph 5 the Examiner asserts that there is no support in the specification for the recitation of the term "simultaneously", however, applicants would like to direct the Examiner's attention to page 8, lines 17-20 where the specification discloses "simultaneous monitoring of a large number of genes" using methods known in the art and described in publications incorporated by reference in the specification. Also, on page 10 lines 10-14, the specification discloses monitoring the expression of one or more maintenance genes along with the expression of a target gene. In addition an example is provided that describes hybridization of nucleic acid samples to a probe array containing probe sets for 7129 genes, see page 12, lines 14-15. It was well known in the art at the time the application was filed that such probe arrays allow simultaneous measurement of expression of hundreds or thousands of genes. Applicants

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respectfully submit that in view of the above remarks, the rejection of claims 12 and 13 under 35 U.S.C. §112, first paragraph, should be withdrawn.

***Claims Rejected Under 35 U.S.C §112, Second Paragraph***

In paragraph 6 the Examiner rejected Claims 12-13 as allegedly being indefinite. Applicants have amended claim 13 to clarify that the claimed method is a method to obtain a normalized expression level for a target gene by adjusting an expression measurement obtained for the target gene using as reference values expression measurements obtained for a selected set of at least ten maintenance genes, selected from a novel set of maintenance genes. Methods of normalizing an experimental value in relation to a reference value are well known in the art, but use of the genes claimed as reference maintenance genes is novel. Support for these amendments to claim 13 may be found on page 10 lines 9-14 and on page 4 line 22 and page 5 lines 1 and 2.

Also in paragraph 7, the Examiner pointed out that the limitation "the expression measurement of said gene" in claim 12 lacked antecedent basis. Applicants have amended claim 13 to clarify that an expression measurement of the target gene is obtained and an expression measurement for each of the at least ten maintenance genes is obtained thus providing antecedent basis for the limitations in claim 12.

Applicants respectfully submit that in view of the above remarks and amendments, the rejection of claims 12 and 13 under 35 U.S.C. §112, second paragraph, should be withdrawn.

***Claims Rejected Under 35 U.S.C §103***

In paragraph 10, the Examiner rejected claims 12 and 13 over MacLeod et al. (U.S. Patent No. 6,221,600 B1) in view of Kagawa et al. (Int. J. Biochem. 20(3):219-29, 1990). MacLeod et al. is cited as teaching methods of normalization by using sets of "housekeeping" genes. MacLeod et al. do not teach measurement of the particular maintenance genes currently claimed. Kagawa et al. is cited as teaching ATP synthases and subunits of ATP synthases as maintenance genes. Applicants have amended claim 13 to delete the recitation of all ATP synthase subunits. Applicants have added several additional genes in place of the ATP synthase related genes. The added genes and where they are supported in the specification are as follows: G Protein Pathway Suppressor 1 (GPS1) is supported at page 44, line 22; Histone class C (H3F2) is supported at page 44, line 38; Proteasome subunit HsC10-II (PSMB3) is supported at page 47, line 31; Nuclear ribonucleoprotein particle (hnRNP) C protein (HNRPC) is supported at page line 48, line 34; ADP-ribosylation factor 1 (ARF1) is supported at page 50, line 37; Integral membrane protein calnexin (CANX) is supported at page 53, line 37; Lysyl-tRNA synthetase (KARS), previously known as KIAA0070, is supported on page 54, line 27; and Esterase D (ESD) is supported at page 56, line 1. Applicants respectfully submit that in view of the above remarks and amendments, the rejection of claims 12 and 13 under 35 U.S.C. §103, should be withdrawn.

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**CONCLUSION**

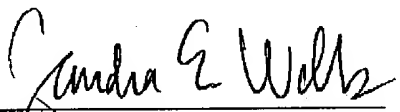
For these reasons, Applicants believe all pending claims are now in condition for allowance. If the Examiner has any questions pertaining to this application or feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Applicants respectfully request that a timely Notice of Allowance be issued in this case.

Date: July 1, 2004

Respectfully submitted,

By   
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